REMARKS

Applicant has carefully reviewed this Application in light of the Office Action mailed March 7, 2006. Applicant has amended Claims 1-2, 5, 7, 9-12, 15, 17, 19-22, 25, 27, and 29-31 and canceled Claims 3-4, 6, 8, 13-14, 16, 18, 23-24, 26, and 28. Applicant respectfully requests reconsideration and allowance of all pending claims.

The Claims Recite Patentable Subject Matter

The Examiner rejects Claims 1-31 under 35 U.S.C. § 101 because "the claimed invention is directed to non-statutory subject matter." According to the Examiner, "[t]he 'calculated repulsion term' identified by the method is not a concrete, tangible, and useful result."

Applicant respectfully disagrees with the Examiner. The *calculated repulsion term* facilitates calculation of a *PMF score of a protein-ligand complex* that indicates a *binding affinity between a protein and a ligand in the protein-ligand complex*, as recited in amended independent Claims 1, 11, 21, and 31.

According to the Federal Circuit, "data, transformed by a machine through a series of mathematical calculations to produce a smooth waveform display on a rasterizer monitor, constitute[s] a practical application of an abstract idea (a mathematical algorithm, formula, or calculation) because it produced 'a useful, concrete and tangible result'—the smooth waveform." *State Street Bank & Trust Co. v. Signature Financial*, 149 F.3d 1368, 1373 (Fed. Cir. 1998). Moreover, "the transformation of electrocardiograph signals from a patient's heartbeat by a machine through a series of mathematical calculations constitute[s] a practical application of an abstract idea (a mathematical algorithm, formula, or calculation) because it correspond[s] to a useful, concrete, or tangible thing—the condition of a patient's heart. *Id.* Furthermore, "the transformation of data, representing discrete dollar amounts, by a machine through a series of mathematical calculations into a final share price, constitutes a practical application of a mathematical algorithm, formula, or calculation because it produces 'a useful, concrete and tangible result'—a final share price momentarily fixed for recording

and reporting purposes and even accepted and relied upon by regulatory authorities and in subsequent trades." *Id.*

In *AT&T Corp. v. Excel Communications, Inc.*, the Federal Circuit held that the following claim "comfortably falls within the scope of § 101":

> A method for use in a telecommunications system in which interexchange calls initiated by each subscriber are automatically routed over the facilities of a particular one of a plurality of interexchange carriers associated with that subscriber, said method comprising the steps of:
> generating a message record for an interexchange call between an originating subscriber and a terminating subscriber, and
> including, in said message record, a primary interexchange carrier (PIC) indicator having a value which is a function of whether or not the interexchange carrier associated with said terminating subscriber is a predetermined one of said interexchange carriers.

172 F.3d 1352, 1354, 1358 (Fed. Cir. 1999). According to the Federal Circuit, the "claimed process employs subscribers' and call recipients' PIC [indicators] as data, applies Boolean algebra to those data to determine the value of the PIC indicator, and applies that value through switching and recording mechanisms to create a signal useful for billing purposes." *Id.* at 1358. The Federal Circuit then went on to hold that the claim at issue was directed to statutory subject matter because "the claimed process applies the Boolean principle to produce a useful, concrete, tangible result without pre-empting other uses of the mathematical principle." *Id.* According to the Federal Circuit, the "useful, concrete, tangible result" of the claimed process was the claimed PIC indicator, which "represents information about the call recipient's PIC, a useful, non-abstract result that facilitates differential billing of long-distance calls made by an IXC's subscriber." *Id.*

Applicant respectfully submits that a *calculated repulsion term* facilitating calculation of a *PMF score of a protein-ligand complex* that indicates a *binding affinity between a protein and a ligand in the protein-ligand complex*, as recited in amended independent Claims 1, 11, 21, and 31, is at least as "useful, concrete, and tangible" as a smooth waveform, electrocardiograph signals, a final share price, or an indication of the primary interexchange carrier of a call recipient.

Accordingly, Applicant respectfully requests reconsideration and allowance of independent Claims 1, 11, 21, and 31 and all their dependent claims.

The Specification Describes Structures for Performing
Functions Recited in the Claims

The Examiner rejects Claims 1-10 and 31 as "failing to comply with the written description requirement." According to the Examiner, "Claim 31 recites various 'means for' clauses. Claims 1-10 recite 'modules that have a certain function and are described only by that function. The means for and 'modules' lack specific related structures in the specification. No specific computer, apparatus, or system structures for performing these means are disclosed." Applicant respectfully disagrees with the Examiner.

Claims 1-2, 5, 7, 9-10, as amended, do not recite any modules. Applicant has canceled Claims 3-4, 6, and 8.

Regarding independent Claim 31, the Specification provides the following description:

> FIGURE 1 illustrates an example system 10 for calculating a PMF score of a protein-ligand complex. System 10 includes a computer system 12 and a PMF-scoring module 14. In particular embodiments, a module may include software, hardware, or both. Computer system 12 may enable a user to provide input to and receive output from PMF-scoring module 14. Computer system 12 may include one or more modules for generating one or more graphical user interfaces (GUIs) for providing input to and receiving output from PMF-scoring module 14. PMF-scoring module 14 may calculate one or more PMF scores of one or more protein-ligand complexes specified by a user and return the calculated PMF scores to the user. A PMF score of a protein-ligand complex may indicate the binding affinity between the protein and the ligand in the protein-ligand complex, and the binding affinity between the protein and the ligand in the protein-ligand complex may indicate the ability of the ligand to inhibit or otherwise modify the function of the protein. PMF-scoring module 14 includes a repulsion-term module 16 that may calculate one or more repulsion terms, as described below. PMF-scoring module 14 may use PMF-scoring data 18 to calculate a PMF score of a protein-ligand complex. PMF-scoring data 18 data that PMF-scoring module 14 may use to calculate a PMF score of a protein-ligand complex. In particular embodiments, PMF-scoring data 18 includes empirically derived

parameters (such as minimum binding-energy distance and well-depth values) that may be used to calculated a PMF score of a protein-ligand complex, as described below. Although components of system 10 are described and illustrated as being separate from each other, the present invention also contemplates any suitable components of system 10 being combined with any other suitable components in any suitable manner. As an example and not by way of limitation, in particular embodiments, PMF-scoring module 14 is executed at computer system 12. As another example, in particular embodiments, PMF-scoring data 18 is stored at computer system 12.

(Specification, Page 5, Lines 2-28). The Specification provides further descriptions of system 10, computer system 12, PMF-scoring module 14, repulsion-term module 16, and PMF-scoring data 18 and their collective and individual functionality. In particular embodiments, system 10, computer system 12, PMF-scoring module 14, repulsion-term module 16, PMF-scoring data 18, or a combination of two or more such structures perform functions recited in Claim 31.

Accordingly, Applicant respectfully requests reconsideration and allowance of independent Claims 1 and 31 and all their dependent claims.

The Claims are Definite

The Examiner rejects Claims 1-10 and 31 as "being indefinite for failing to particularly point out and distinctly claim the subject matter of which applicant regards as the invention." According to the Examiner, independent Claim 31 recites "various 'means for' clauses. Claims 1-10 recite 'modules' for performing functions. The specification as filed does not set forth specific structures for performing the means recited. The means for and modules all lack specific related structures in the specification." Applicant respectfully disagrees with the Examiner. Claims 1-2, 5, 7, 9-10, as amended, do not recite any modules, and Applicant has canceled Claims 3-4, 6, and 8. Moreover, as Applicant has demonstrated above, the Specification describes structures for performing the functions recited in independent Claim 31.

The Examiner further rejects Claims 1-31 as "being indefinite for failing to particularly point out and distinctly claim the subject matter of which applicant regards as the

invention." According to the Examiner, "it is entirely unclear what the system comprises." Although Applicant respectfully disagrees with the Examiner, to facilitate issuance of a Patent from this Application, Applicant has made clarifying amendments to Claims 1-2, 5, 7, 9-12, 15, 17, 19-22, 25, 27, and 29-31 and canceled Claims 3-4, 6, 8, 13-14, 16, 18, 23-24, 26, and 28.

The Examiner states, "It is entirely unclear how the limitation of claim 10 (the genetic algorithm) modifies the system of claim 9, or any preceding claim." Applicant respectfully disagrees with the Examiner. Dependent Claim 9, as amended, recites that *the first set of empirically derived minimum binding-energy distances and well-depth values or second sets of empirically derived minimum binding-energy distances and well-depth values are each a product of one or more manual processes or automatic processes*. Dependent Claim 10, as amended, recites that *at least one of the automatic processes comprises execution of a genetic algorithm*. Dependent Claims 29-30 recite limitations similar to the limitations recited in dependent Claims 9-10.

According to the M.P.E.P., "breadth of a claim is not to be equated with indefiniteness." M.P.E.P. ch. 2173.04 (Rev. 3, August 2005). "If the claims, read in light of the specification, reasonably apprise those skilled in the art . . . of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, [35 U.S.C. § 112 para. 2] demands no more." M.P.E.P. ch. 2173.05(a)(II) (Rev. 3, August 2005). Similarly, if a claim is directed to patentable subject matter, the claim is allowable if it "define[s] the patentable subject matter with a reasonable degree of particularity and distinctness." M.P.E.P. ch. 2173.02 (Rev. 3, August 2005) (emphasis in original). "Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire." *Id.* The M.P.E.P. also states:

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
> (A) The content of the particular application disclosure;
> (B) The teachings of the prior art; and
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Id.

Applicant respectfully submits that dependent Claim 10 at least reasonably apprises those skilled in the art of the use and scope of the invention and that dependent Claim 10 is at least as precise as the subject matter permits.

The Specification provides the following description of an example use of a genetic algorithm:

> As an example and not by way of limitation, in particular embodiments, a first set of minimum binding-energy distance and well-depth values is generated. Each atom-pair type has a minimum binding-energy distance value and a well-depth value in a generated set of minimum binding-energy distance and well-depth values. One or more of the values in the first set may be generated manually. One or more of the values in the first set may be generated automatically. One or more of the values in the first set may be generated according to a random process (such as a genetic algorithm). A genetic algorithm may be executed automatically by a computer system. The first set of minimum binding-energy distance and well-depth values is then used to calculate a PMF score of each of multiple protein-ligand complexes. The calculated PMF scores are then used to predict the structure of each of the protein-ligand complexes.

(Specification, Page 10, Lines 12-23). The Specification also provides the following description of another example use of a genetic algorithm:

> One or more of the values in the second set of values may be generated manually. As an example and not by way of limitation, a user may review the results of the first set of values and modify one or more minimum binding-energy distance values, well-depth values, or both in the first set of values to generate the second set of values. One or more of the values in the second set of values may be generated automatically. One or more of the values in the second set of values may be generated according to a random process (such as a genetic algorithm). As an example and not by way of limitation, a genetic algorithm may be applied to the first set of values to generate the second set of values.

(Page 11, Line 24, through Page 12, Line 2).

Accordingly, Applicant respectfully requests reconsideration and allowance of Claims 1-2, 5, 7, 9-12, 15, 17, 19-22, 25, 27, and 29-31.

Independent Claims 1, 11, 21, and 31 are Allowable over *Muegge*

The Examiner rejects independent Claims 1, 11, 21, and 31 under 35 U.S.C. § 102(b) as being anticipated by *A General and Fast Scoring Function for Protein-Ligand Interactions: A Simplified Potential Approach* by Ingo Muegge and Yvonne C. Martin ("*Muegge*"). *Muegge* merely discloses using only collected observations of protein-ligand atom distances to derive a new scoring function. (Page 793, Column 1). *Muegge* ignores all other structural information. *Id.*

In contrast, independent Claim 1, as amended, recites:

An apparatus comprising:
one or more processors; and
a memory coupled to the processors comprising one or more instructions, the processors operable when executing the instructions to:
determine an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;
calculate a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type;
calculate a potential of mean force (PMF) of the protein-ligand atom pair according to the calculated repulsion term of the protein-ligand atom pair; and
calculate a PMF score of the protein-ligand complex according to the calculated PMF of the protein-ligand atom pair, the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex.

Independent Claims 11, 21, and 31 recite limitations similar to the limitations recited in independent Claim 1.

Muegge fails to disclose, teach, or suggest ***calculating a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type***, as recited in independent Claim 1. The Examiner asserts that the ligand volume correction factor in *Muegge* can be properly considered ***a well-depth value of the atom-pair type***, as recited in independent Claim 1. Applicant respectfully disagrees with the Examiner. Nowhere does *Muegge* disclose, teach, or suggest that the ligand volume correction factor in *Muegge* is a ***well-depth value***, as recited in independent

Claim 1. Moreover, even assuming for the sake of argument that the ligand volume correction factor in *Muegge* were a **well-depth value**, as recited in independent Claim 1, *Muegge* would still fail to disclose, teach, or suggest a ligand volume correction factor **of an atom-pair type**, as recited in independent Claim 1. Instead, *Muegge* indicates that the ligand volume correction factor corresponds to a ligand atom type, not to **an atom-pair type of a protein-ligand atom pair**, as recited in independent Claim 1. *Muegge* uses the notation i and j to represent protein atom type and ligand atom type, respectively, and describes the ligand volume correction factor as $f_{Vol\_corr}^{j}(r)$, which excludes any reference to protein atom type. (Page 793, Column 2).

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); M.P.E.P. ch. 2131 (Rev. 1, Feb. 2003) (Quoting *Verdegaal Bros.*, 2 U.S.P.Q.2d at 1053). Moreover, "the identical invention must be shown in as complete detail as is contained . . . in the claim." *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989); M.P.E.P. ch. 2131 (Rev. 1, Feb. 2003) (Quoting Richardson, 9 U.S.P.Q.2d at 1920). Furthermore, "[t]he elements must be arranged as required by the claim." *In re Bond*, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990); M.P.E.P. ch. 2131 (Rev. 1, Feb. 2003) (Quoting *In Re Bond*, 15 U.S.P.Q.2d at 1566). As shown above, *Muegge* fails to disclose, either expressly or inherently, each and every limitation recited in independent Claim 1. Therefore, *Muegge* does not anticipate independent Claim 1 under governing Federal Circuit case law and the M.P.E.P.

For at least the above reasons, Applicant respectfully requests reconsideration and allowance of independent Claims 1, 11, 21, and 31 and all their dependent claims.

Independent Claims 1, 11, and 31 are Allowable over *Mitchell*

The Examiner rejects independent Claims 1, 11, and 31 under 35 U.S.C. § 102(b) as being anticipated by *BLEEP—Potential of Mean Force Describing Protein-Ligand Interactions: I. Generating Potential* by John B.O. Mitchell, Roman A. Laskowski, Alexander Alex, and Janet M. Thornton ("*Mitchell*"). *Mitchell* merely discloses a set of pair

potentials derived from high-resolution X-ray structures of protein-ligand structures in the Brookhaven Protein Data Bank (PDB). (Abstract).

In contrast, independent Claim 1, as amended, recites:

> An apparatus comprising:
> one or more processors; and
> a memory coupled to the processors comprising one or more instructions, the processors operable when executing the instructions to:
>> determine an atom-pair type of a protein-ligand atom pair in a protein-ligand complex;
>> calculate a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type;
>> calculate a potential of mean force (PMF) of the protein-ligand atom pair according to the calculated repulsion term of the protein-ligand atom pair; and
>> calculate a PMF score of the protein-ligand complex according to the calculated PMF of the protein-ligand atom pair, the PMF score indicating a binding affinity between a protein and a ligand in the protein-ligand complex.

Independent Claims 11, 21, and 31 recite limitations similar to the limitations recited in independent Claim 1.

Mitchell fails to disclose, teach, or suggest *calculating a repulsion term of the protein-ligand atom pair according to a minimum binding-energy distance value and a well-depth value of the atom-pair type*, as recited in independent Claim 1. The Examiner asserts that the attractive well of the interaction potential between two neon atoms in *Mitchell* can be properly considered *a well-depth value of the atom-pair type*, as recited in independent Claim 1. Applicant respectfully disagrees with the Examiner. Even assuming for the sake of argument that the attractive well of the interaction potential between two neon atoms could be properly considered a *well-depth value*, as recited in independent Claim 1, *Mitchell* would still fail to disclose, teach, or suggest *calculating a repulsion term of a protein-ligand atom pair according to . . . a well-depth value of the atom-pair type of the protein-ligand atom pair*, as recited in independent Claim 1. Instead, *Mitchell* uses the same attractive well—the attractive well of the interaction potential between two neon atoms—to

calculate a reference potential for all atom-type pairs in the set. (Page 1171, Column 2). According to *Mitchell*:

> We know that the short-range repulsive region of the potential is not sampled by the data. Given our expectation that the average energy will have a repulsive wall close to the sum of typical van der Waals radii, we simply import such a function from elsewhere and use it as the reference potential. Because BLEEP largely describes first-row atoms, the neon-neon interaction potential of Ng et at., shown in Figure 1, seems a reasonable choice for this purpose.

Id.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); M.P.E.P. ch. 2131 (Rev. 1, Feb. 2003) (Quoting *Verdegaal Bros.*, 2 U.S.P.Q.2d at 1053). Moreover, "the identical invention must be shown in as complete detail as is contained . . . in the claim." *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989); M.P.E.P. ch. 2131 (Rev. 1, Feb. 2003) (Quoting Richardson, 9 U.S.P.Q.2d at 1920). Furthermore, "[t]he elements must be arranged as required by the claim." *In re Bond*, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990); M.P.E.P. ch. 2131 (Rev. 1, Feb. 2003) (Quoting *In Re Bond*, 15 U.S.P.Q.2d at 1566). As shown above, *Mitchell* fails to disclose, either expressly or inherently, each and every limitation recited in independent Claim 1. Therefore, *Mitchell* does not anticipate independent Claim 1 under governing Federal Circuit case law and the M.P.E.P.

For at least the above reasons, Applicant respectfully requests reconsideration and allowance of independent Claims 1, 11, 21, and 31 and all their dependent claims.

Conclusion

For at least the foregoing reasons, Applicant respectfully requests allowance of all pending claims.

If a telephone conference would advance prosecution of this Application, Applicant invites the Examiner to call Travis W. Thomas, attorney for Applicant, at 214.953.6676.

Please charge $1,020.00 to Deposit Account No. 02-0384 of Baker Botts L.L.P. for a three-month extension of time. The Commissioner is authorized to charge any fee and credit any overpayment to Deposit Account No. 02-0384 of Baker Botts L.L.P.

Respectfully submitted,

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